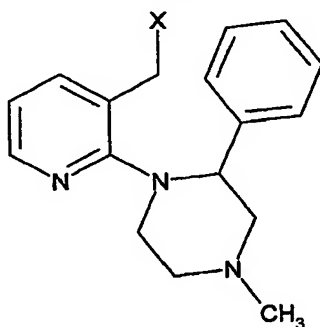


CLAIMS

1. A method for the preparation of enantiomerically pure mirtazapine, said method comprising a step of ring closure of a compound according to formula (II)



(II)

- 5 wherein X is a leaving group, said step comprising treatment with an acid, characterised in that mirtazapine with enantiomeric excess is formed by the ring closure of the compound of formula (II) with enantiomeric excess by treatment with a suitable acid in the absence of a solvent or a suitable combination of an acid and an organic solvent.
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2. The method of claim 1, characterised in that the ring closure occurs using a suitable acid in the absence of a solvent.
- 15 3. The method of claim 2, characterised in that the acid is a protic acid or a protic acid derivative.
4. The method of claim 3, characterised in that the acid is polyphosphoric acid or phosphorus pentoxide in phosphoric acid.
- 20 5. The method according to claim 4, characterised in that the weight ratio between polyphosphoric acid and the compound according to formula II is less than 5 to 1.
6. The method of claim 1, characterised in that ring closure occurs using a suitable acid and organic solvent combination.
- 25 7. The method of claim 6, characterised in that the suitable acid and organic solvent combination is a protic acid or protic acid derivative in combination with a polar coordinating solvent.

8. The method of claim 6, characterised in that the suitable acid and organic solvent combination is a mineral acid in combination with a polar coordinating solvent.
- 5 9. The method of claim 7, characterised in that the suitable acid and organic solvent combination is polyphosphoric acid in combination with *N*-methylpyrrolidinone or DMF.
10. A method for the selection of an acid or an acid/solvent combination suitable for a stereospecific ring closure reaction of an enantiomerically pure compound according to the formula II and meaning of X of claim 1 leading to enantiomerically pure mirtazapine comprising testing the reaction by treatment of the enantiomerically pure compound with a candidate acid or a candidate acid/solvent combination and determining a loss of enantiomeric excess by the reaction and identifying an acid or an acid/solvent combination, as suitable if it results in the loss of less than 40%.
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